

### **REMARKS**

By this amendment, Applicants have amended the specification to insert a "Cross Reference To Related Applications" section. Claim 59 has been amended to include that probes are used that have the same nucleotide sequence and only single nucleotide polymorphisms are analyzed. Support for these amendments can be found in the specification, for example, at page 11, lines 5-16, page 12, lines 5-8, Table 1 and Figure 6. Claim 60 has been amended to independent form as the Examiner considered this claim to be allowable if rewritten in independent form. Thus, Applicants have rewritten claim 60 in independent form using previously presented base claim 59. No new matter has been added. Applicants respectfully request entry of this amendment and reconsideration of the application.

### **Allowable Subject Matter**

Applicants thank the Examiner for indicating that claim 60 would be allowable if rewritten in independent form. In response, Applicants have amended claim 60 to independent form.

### **Rejections Under 35 U.S.C. § 112, First Paragraph: Enablement**

The Examiner rejected claims 32-59 and 61 under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Examiner has the initial burden of presenting showing that the application does not teach how to make and use the invention. *In re Oetiker*, 977 F.2d 1443 (Fed. Cir. 1992). Applicants respectfully submit that the Examiner has not met the burden.

The Examiner alleges that "said six examples do not provide adequate written description of the claimed method whereby one would be able to determine any and all single nucleotide polymorphisms in **any and all species of mammals**". (Office Action, page 6, emphasis added). The Examiner appears to suggest that the claims are enabled

only for the examples disclosed and the claims should be narrowed to cover the examples only.

Applicants respectfully disagree. To restrict [a patentee] to the examples disclosed would be a poor way to stimulate invention, and particularly to encourage its early disclosure. To demand such restriction is merely to state a policy against broad protection for pioneer inventions. *In re Hogan*, 559 F.2d 595, 606 (C.C.P.A. 1977), and *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1287, 1292 (D. Del. 1987), *aff'd*, 865 F.2d 1247 (Fed. Cir. 1989).

Moreover, Applicants respectfully disagree with the Examiner's interpretation of the claims and point out that one of ordinary skill in the art would not interpret the claims in the manner that the Examiner does. Claims 32-59 and 61 include methods for identifying single nucleotide polymorphic sites in the genome of mammals of the **same species**, not different species. Further, claims 49-50, 52, and 55 are specifically directed to horses and Claims 56-58 are specifically directed to horses of the same breed. Thus, the Examiner's interpretation of the claims is untenable.

Applicants respectfully submit that the specification fully enables the claims. In the specification the inventors teach the advantages of using SNPs as genetic markers over other types of polymorphisms including restriction fragment length polymorphisms (RFLPs), STRs (short tandem repeats), variable number tandem repeats (VNTRs). First, SNPs occur with greater allelic frequency and uniformity and thus can be linked to an individual trait (e.g., to identify an individual, parentage, etc.). Second, SNPs are more stable than other classes of polymorphism (e.g., VNTRs, STRs, RFLPs) and not subject to spontaneous mutation like other polymorphisms. Third, a SNP's allelic frequency can be inferred from a small number of representative samples. Fourth, SNPs allow a high degree of genetic information (e.g., base position and location) unlike other types of polymorphisms (see the specification at pages 13-15).

At page 37-45, and Examples 4 and 5 the inventors teach how SNPs can be used to determine, among other things, parentage and identity. Although, Examples 4 and 5 were conducted in horses, the same method can be conducted in mammals of the same

species, and the specification clearly describes this, for example, at pages 4, lines 13-16, page 44 lines 29-36.

Applicants have also amended the claims to include that polymorphic sites comprises a SNP, and the polymorphic site is immediately flanked by a 3' and 5' invariant nucleotide sequence and that the polymorphic sites correspond to the same location of the genome. Thus, the method utilizes specific types of SNPs at the same corresponding location on the genome or locus. Moreover, Examples 1-5 alone utilize 18 polymorphic loci in sixty horses, over 1,000 SNPs utilized in the method. Applicants submit the specification provides fully enables the claims. The specification at pages 13-15, page 44, lines 29-36 and Examples 1-6 clearly discloses and enables conducting genetic analysis using SNPs from mammalian DNA of the same species.

The Examiner asserts that the specification “does not provide adequate written description of how to practice the full scope of the invention where but one strand is analyzed...” (Office Action, page 6). Applicants respectfully submit that claim 59 specifically recites that upper and lowers strands are analyzed and Applicants respectfully submit that the enablement rejection should be withdrawn with respect to at least claim 59.

The Examiner also asserts that “in view of the agreement that the claims do encompass such an embodiment, and that the technology was developed until about 9 years post filing of the priority date of the instant application, it is not possible for applicant to have enabled such.” (Office Action, page 10). Applicants respectfully disagree with the Examiner’s assertions and submit that future improvements can be covered by earlier filed patents. *See, for example, Laser Alignment, Inc. v. Woodruff & Sons, Inc.*, 491 F.2d 866 (7th Cir. 1974) (finding that a patent on using a beam of light to align pipe covered the use of a laser to align pipe, even though the laser had not been developed when the invention was made); *Chiron Corp. v. Genentech, Inc.*, 266 F. Supp. 2d 1172 (E.D. Cal. 2002) (interpreting a patent that, when written in 1984, covered only mouse-derived antibodies, to cover all sorts of antibodies developed between 1984 and 1999, including chimeric and humanized antibodies). Applicants respectfully submit

that the Examiner is using improper hindsight to interpret the claims by requiring disclosure for simultaneous sequencing in the specification.

The Examiner relies, among other things, on *Genentech v. Novo Nordisk* (“*Genentech*”) for his enablement rejection. As previously argued in the prior response, the Examiner's reliance on *Genentech* as analogous to the present case is misplaced. *Genentech* was decided on strikingly different facts. In *Genentech*, the claims recited a method for making human growth hormone in a fusion protein and cleaving the fusion protein to make the growth hormone. The patentees in *Genentech* tried to rely on the level of skill in the art to enable the claim, but at the time of filing the application it was **not** known in the art how to cleave a fusion protein to make growth hormone, **where the cleaving of the fusion protein was the novel aspect of the claim**. In contrast, the novel aspect of the amended claims does not include claims to individual SNPs, but methods using the combinations of SNPs as useful genetic markers. Thus, *Genentech* sheds no light on any alleged written description or enablement issues with respect to the present claims. *Genentech* is simply inapplicable to the facts of this case.

Moreover, claim 59 includes that the starting material involves known SNPs to determine the parentage testing. It is respectfully submitted, that the starting material is clearly provided by the specification. Applicants submit that the specification fully complies with the enablement requirement for methods of identifying and characterizing single nucleotide polymorphic sites in the genome of mammals of the same species. Accordingly, Applicants respectfully request withdrawal of this rejection.

#### **Rejection Under 35 U.S.C. § 101**

Claims 32-45, 48 and 51-55 are rejected under 35 U.S.C. § 101 as allegedly not supporting a specific, substantial and credible utility. Applicants respectfully traverse this rejection.

The Examiner has the initial burden of showing that the specification is not directed to a specific, substantial and credible utility. *In re Brana*, 34 USPQ2d at 1441 (Fed. Cir. 1995). *In re Langer*, 183 USPQ 288 (CCPA 1974). Applicants respectfully submit that the Examiner has not met this burden.

In the specification the inventors teach the advantages of using SNPs as genetic markers over other types of polymorphisms including restriction fragment length polymorphisms (RFLPs), STRs (short tandem repeats), variable number tandem repeats (VNTRs). SNPs occur with greater allelic frequency and uniformity and thus can be linked to an individual trait (e.g., to identify an individual, parentage, etc.). SNPs are more stable than other classes of polymorphism (e.g., VNTRs, STRs, RFLPs) and not subject to spontaneous mutation like other polymorphisms. A SNP's allelic frequency can be inferred from a small number of representative samples. SNPs allow a high degree of genetic information (e.g., base position and location) unlike other types of polymorphisms (see the specification at pages 13-15). At page 37-45, and Examples 4 and 5 the inventors teach and show how SNPs can be used to determine, among other things, parentage and identity. Applicants respectfully submit that one of ordinary skill in the art would conclude that specific, substantial and credible utilities are clearly described and claimed. Accordingly, Applicants respectfully submit that the claims fully comply with 35 U.S.C. §101 and request withdrawal of this rejection.

**Rejections under 35 U.S.C. §103(a)**

The Examiner rejects claims 32-36, 38-43, 45-46, 48, 51, 53, 54, and 59 under 35 U.S.C. §103(a) as allegedly being obvious over *Eur. J. Immunogenet.* 18:33-55 (1991) (Erlich). The Examiner also rejects claims 33-35 and 39-55 under 35 U.S.C. §103(a) as allegedly being obvious over Erlich in view of *Swiss Medical Weekly* 119:815-825 (1989) (Fey). Applicants respectfully traverse these rejections.

A prior art reference cannot render an invention obvious if the reference teaches away from the claimed invention. *KSR International Co. v. Teleflex Inc.* 127 S. Ct. 1727, 1734. Applicants respectfully submit that neither Erlich nor Fey make obvious methods of using a panel of SNPs to determine allelic frequency, parentage and identity among mammals of the same species.

In the Office Action, the Examiner alleges that Erlich shows a method of identifying SNPs in a genome of interest, particularly in 18 different sequences (Office

Action, item 28 on page 13). The Examiner refers to Figure 1-3 and Table 1 of Erlich in support of his position. Applicants respectfully disagree with the Examiner.

Erlich teaches typing the HLA gene using allele specific oligonucleotide probes (ASO) that hybridize to HLA class II polymorphisms DQA1, DQB1, DRB1, and DPB1. These HLA class II polymorphisms are polymorphic regions and not single nucleotide polymorphisms. The allele specific probes listed in Table 1, which the Examiner refers to, do not discriminate among alleles that differ by a single nucleotide base. If the ASO probes did, they would differ by one nucleotide base as well. Figure 3, which the Examiner also refers to, illustrates the DNA sequence and probe alignments for the probes listed in Table 2. Note the DNA locus and probe alignments listed in Table 2 of Erlich and the regions he interrogates have multiple nucleotide variations and could not and are not considered single nucleotide polymorphisms that are immediately flanked by a 3' and 5' invariant nucleotide sequence as currently claimed.

In contrast to SNPs, Erlich teaches polymorphic regions containing at least 2 to 3 nucleotide variations:

The allelic diversity at the DPB1 locus presents more of a challenge for oligonucleotide probe typing because of the dispersed nature of the **polymorphic sequences** (Fig. 3). The second exon contains six variable regions (A to F) with a limited number of **polymorphic residues (n=2-3) at each position** (Erlich, at page 37, emphasis added).

Erlich's ASO probes each are directed against a specific allele having a polymorphic region that is arrayed and exposed to PCR amplicons generated by the sample, and it is the pattern on the array that reveals the genotype:

Our approach has been to use a panel of 15 oligonucleotide probes (listed in Table 2) specific for the sequence variants in four polymorphic regions with the pattern of probe hybridization identifying a specific DPB allele (see Table 3). (Erlich, at page 40).

Thus, it is the pattern of matching ASOs with sample amplicons, where the amplicons are of polymorphic regions, not SNPs that identifies genotypes. Accordingly, Erlich teaches trait association by polymorphic region, not by SNPs.

Fey, like Erlich, does make the pending claims obvious. Fey teaches two different types of polymorphisms: (1) RFLPs and (2) highly variable regions (HVRs)-- which is a type of VNTR. These types of polymorphisms are discussed on pages 2 and 3 of the specification. And again, one of ordinary skill in the art would not consider these types of polymorphisms SNPs.

Moreover, Applicants submit that before the filing of the present application, one of ordinary skill in the art would not consider using a panel of SNPs as genetic markers and would not have recognized that SNPs could provide valuable genetic information including, among other things, determining allelic frequency, parentage and identity among mammals of the same species.

Because Erlich and Fey teach away from methods of using a panel of SNPs to determine, among other things, allelic frequency, parentage and identity among mammals of the same species, Applicants respectfully submit that the present claims cannot be considered obvious. Accordingly, Applicants respectfully request withdrawal of the rejections.

The Examiner asserts that the claims do not require the use of the same probes and "that one only be looking for a single nucleotide polymorphism." (Office Action, page 16, item 38). Applicants have amended claim 59 to include that the identification utilizes probes that have the same nucleotide sequence and that only single nucleotide polymorphisms are analyzed. Thus, Applicants respectfully submit that the obviousness rejection should be withdrawn with respect to at least claim 59.

**Conclusion**

Reconsideration and allowance are respectfully solicited.

Applicants hereby requests a three-month extension of time under 37 CFR 1.136(a) and authorizes the Patent Office to charge the Deposit Account No. 11-0171. If any additional fees are due, or an overpayment has been made, please charge, or credit, our Deposit Account No. 11-0171 for such sum.

If the Examiner has any questions regarding the present application, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,

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